# Section V: Status of Mental Health Services

## Chapter 15

# Antipsychotic Medication Utilization in a State Mental Hospital System, 1994–2000*

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## Introduction

This chapter describes antipsychotic prescribing practices in a large State hospital system from 1994 to 2000. During this seven-year period, the introduction of newer atypical medications has greatly expanded the antipsychotic armamentarium. We will characterize how antipsychotic prescribing patterns have changed since 1994 with regard to the medications used, their typical dosages, and how they are combined with other antipsychotic medications. We will use data from 1999 to provide detailed information on patient characteristics that correlate with anti-psychotic medication use.

Both methodological and informatics challenges arise in accurately presenting prescribing data or prescribing practices, especially for long-term patients, who often receive multiple medications sequentially or simultaneously. Considerations include the characteristics and limitations of the data source used; choices regarding the period of time sampled (e.g., one year vs. one quarter vs. one day of prescribing); and choices regarding the relevant unit of analysis, that is, the prescription or the patient. Likewise, when reporting over a seven-year period, the underlying study population is subject to change, and these changes must be described to fully understand the context of prescribing practices.

## Study Methodology and Methodologic Issues

### Use of Clinical Database

We examined all antipsychotic prescriptions written for inpatients in the adult civil hospitals in the State-run mental hospital system of New York for the period from January 1, 1994, to December 31, 2000. Prescription records are maintained in the Integrated Research Database (IRDB) created by the Information Systems Division of the Nathan Kline Institute for Psychiatric Research. The IRDB contains patient information (demographic charac-

* Maintenance of the Integrated Research Database of the Nathan S. Kline Institute for Psychiatric Research is supported by grants from Pfizer, Eli Lilly and Co., and the Janssen Research Foundation. Ari Jaffe receives support from National Institute of Mental Health training grant R25 MH60496.

teristics, dates of admission/transfer/discharge, and diagnosis) and drug prescription information for every inpatient within all adult civil facilities of the New York State Office of Mental Health (OMH) hospital system. The prescription information includes drug, dosage, and duration of order. A clinical database such as the IRDB offers several advantages for a study of medication prescribing (Tierney and McDonald, 1991). First, it provides relatively accurate and timely data. Because medication prescribing information in the IRDB is derived from the same clinical system used by the hospitals' pharmacists for dispensing purposes, pharmacists have a strong clinical interest in catching and correcting data entry errors. In the New York State system, the requirement that physicians actively reorder medication on a monthly basis provides a further check on the accuracy of prescribing data for medication episodes that last more than one month. Second, the integration of diagnostic, demographic, and admission/discharge information in the same database as prescribing information provides the opportunity for more detailed patient-based analysis than, for example, outpatient claims data. Third, State hospitals have the advantage of being a "closed system," in which all prescribing events for individual patients are sure to be captured and within which medication compliance, although far from certain or complete, is likely to be higher than in the community.

## Time Period Sampled

Some reports in the literature of medication utilization rely on single-day surveys of active prescriptions (Michel and Kolakowska, 1981; Muijen and Silverstone, 1987; Schmidt et al., 1987; Tibaldi et al., 1997). This is a convenient strategy in situations where an analysis of prescribing practices requires an exhaustive manual search of prescribing records or the completion of a large cross-sectional survey. This strategy, however, considers only a fraction of the prescribing occurring in a given system. Furthermore, when an analysis of prescribing is extended beyond a simple account of use, such as in calculations of medication episode length or in an assessment of antipsychotic combination therapy, a snapshot of a single day can be misleading. For example, a single-day analysis will fail to distinguish between deliberate coprescribing (the simultaneous, intentional prescribing of two antipsychotics) and medication overlaps that occur because of medication cross-tapers. We therefore chose to count all prescriptions in the OMH database.

## Unit of Reporting

Another methodological consideration is whether to report utilization data based on *patients* or based on *prescriptions (medication episodes)*. The advantages of reporting based on patients (i.e., what percentage of patients received one or another particular medication) are obvious: The results are intuitive; the patient is the most clearly identifiable and relevant object of clinical interest; and basing the calculations on people allows for simpler correlation with other person-based data, such as demographic and diagnostic information. However, significant problems are also associated with this method of reporting. First, in such an analysis, patients receiving multiple medications—either simultaneously or in sequence—would be duplicated, once for each of the medications they receive. As a result, patients receiving all medications would sum to greater than 100 percent. Second, the use of the patient as the object of study eliminates possibilities for examining the temporal aspects of prescribing, in terms of both the duration of a given medication regimen and the sequence in which particular regimens are prescribed. For these reasons, we chose to report most of our findings on the basis of the total number of antipsychotic medication episodes ordered during the period under study.

Individual medication prescribing episodes were defined as the period during which a particular antipsychotic was ordered for a given patient. Dose changes and medication renewals did not trigger the counting of a new episode. Thus, an episode was counted as the time between the first prescription for a given medication and its final discontinuation. Gaps of fewer than four days between individual medication episodes for the same medication led to linking the episodes into a single, longer episode. Only episodes with a length of seven days or more were included in the analyses. When two or more anti-psychotic medications were administered simultaneously for more than seven days, they were counted as a "coprescribing" episode.

## Classes of Antipsychotic Medications

To simplify the reporting of antipsychotic medication utilization, we classify antipsychotics into three classes: (1) atypical, (2) oral typical, or (3) de-

Table 1. Classes of antipsychotic medication

| Typicals | Depots | Atypicals |
|---|---|---|
| Chlorpromazine | Haloperidol Decanoate | Clozapine *(marketed U.S. 1990)* |
| Fluphenazine | Fluphenazine Decanoate | Risperidone *(marketed 1994)* |
| Haloperidol | | Olanzapine *(marketed 1996)* |
| Loxapine | | Quetiapine *(marketed 1997)* |
| Mesoridazine | | |
| Molindone | | |
| Perphenazine | | |
| Thioridazine | | |
| Thiothixine | | |
| Trifluorperazine | | |

pot. Table 1 indicates the medications included in each class. For many analyses, we considered clozapine separately from the other atypical medications because, although clozapine became available several years earlier than the other atypicals, there were initially restrictions on its use. Later, an internal policy was implemented to promote its use among refractory patients.

### Medication Dose

Reporting on medication dose data for a population of patients over a continuous period poses challenges of its own because different patients receive different doses over different periods of time. Thus, one way to report average medication dose is as *the mean daily patient dose*—that is, the total dose of each medication *for each patient* across a prescribing episode divided by the length of the episode. Another way to report is by using the *mean dose weighted by days*—the total dose of each medication *for all patients* receiving that medication during the observation period divided by the total number of drug days for that medication. The former number is more indicative of how the "average" patient is treated with a particular medication, whereas the latter number is more indicative of how a particular medication is used overall. Therefore, mean dose weighted by days is the method used in this report.

## Context/Study Population

The New York State OMH currently operates 17 adult civil facilities (two others have closed since 1994). From 1994 to 2000, these facilities for the most part ceased taking admissions directly from the community. With the exception of patients requiring readmission within two months of their discharge from a State facility, the acutely mentally ill are now hospitalized first in community facilities. Referral for further care in a State facility for nonresponsive patients can begin approximately three weeks after community admission, but most patients are hospitalized in the community for close to 60 days prior to their transfer. As a consequence, our study population is enriched for patients who would be considered relatively refractory in other treatment contexts.

The period studied was a time of contraction for the inpatient State hospitals operated by the New York State OMH, with the total bed census dropping from 8,459 at the end of the first quarter of 1994 to 4,528 7 years later. As illustrated in figure 1, the proportion of patients who received some antipsychotic treatment remained relatively stable, rising only slightly from 84 to 89 percent over the period. Figure 1 also illustrates that despite the overall decline in the patient population, the distribution of lengths of stay among patients receiving antipsychotic medication was largely stable. Despite changes in the referral process previously described, admissions continued to constitute 15 to 20 percent of the total patient population in any given quarter during the study period. The proportion of patients with lengths of stay between 90 days and one year remained between 22 and 30 percent during the period, and a substantial portion of the hospitalized population (50 to 60 percent) were long-stay patients, with lengths of stay of more than one year.

For 1999, characteristics of admissions (48 percent) and patients already in the hospital as of January 1, 1999—residents—(52 percent) are described in table 2. The resident population reflects the long-stay group, with a mean length of stay of more than six years. One year later, only 39.5 percent of this group had been discharged from the hospital. Newly admitted patients, by contrast, had a mean length of stay of 145.7 days and an 82.5 percent probability of discharge within one year of admission. Thus, one

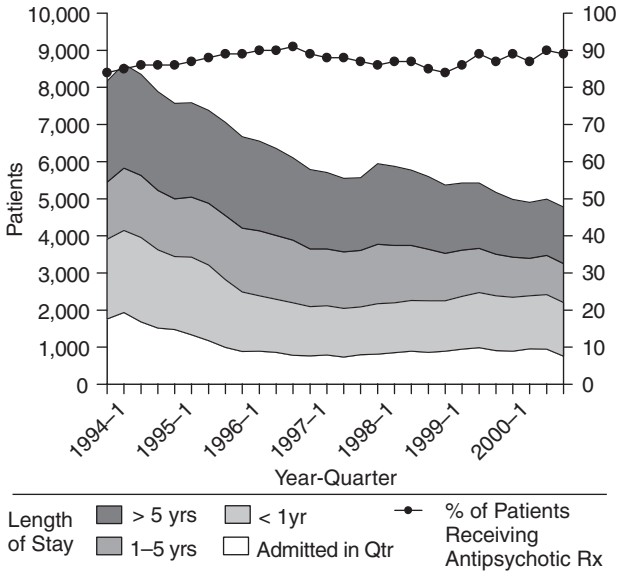


Figure 1. Patients Receiving Antipsychotics, 1994–2000 (only patients receiving at least 7 days of antipsychotics counted).

group of patients cycles in and out from the community with relatively short stays and a relatively high likelihood of discharge. Another group has much longer stays and a low likelihood of discharge. Failure of the long-stay patients to be discharged likely reflects, at least in part, their greater resistance to usual pharmacotherapy strategies. They might, therefore, be expected to differ from shorter-stay patients in terms of medication utilization.

From 1994 to 2000, the diagnostic characteristics of the patient population remained largely stable, although there was a modest trend toward a larger proportion of patients with a diagnosis of schizophrenia or schizoaffective disorder (68 percent in 1994, rising to 79 percent in 2000). During the same period, within the schizophrenia/schizoaffective subgroup, the proportion diagnosed as schizoaffective rose from 24 to 32 percent.

# Trends in Prescribing Practices

## Types of Antipsychotics Prescribed

As indicated in figure 2, the most common antipsychotic prescribing regimen in 1994 was treatment with a single oral typical agent. This form of prescribing dropped precipitously in the period under study, from 70.2 percent of prescribing episodes at the start of 1994 to 10.3 percent of prescribing episodes at the end of 2000. Over the same period, the use of atypical medications rose dramatically. At the start of 1994, 8.6 percent of medication episodes used an atypical medication singly or in combination. By the end of 2000, 78.7 percent of episodes used an atypical agent. Figure 3 illustrates the use of the individual atypical agents (the already introduced clozapine and the newer agents risperidone, olanzapine, and quetiapine), showing the proportion of medication episodes that used each atypical during the indicated quarter. As each new medication was introduced, a period of adjustment in the mean prescribed daily dosage was observed (see figure 4). For both quetiapine and olanzapine, this was a period characterized by a large increase in total daily dose. Risperidone experienced an initial increase in mean dose, followed by a decline.

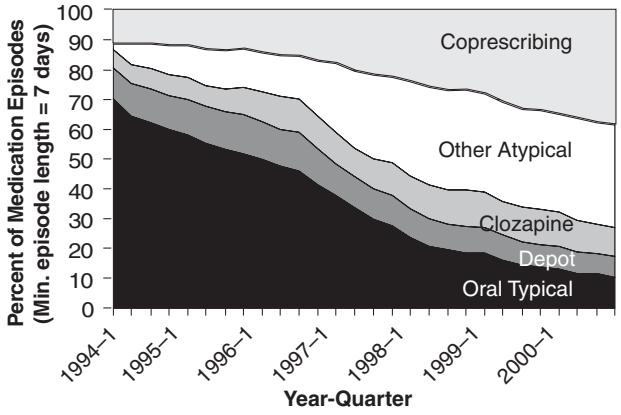


Figure 2. Antipsychotic Medication Utilization, 1994–2000.

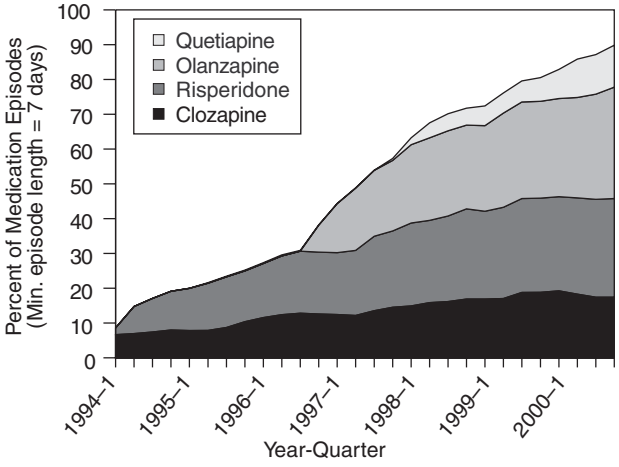


Figure 3. Introduction of Atypical Antipsychotic Medication, 1994–2000.

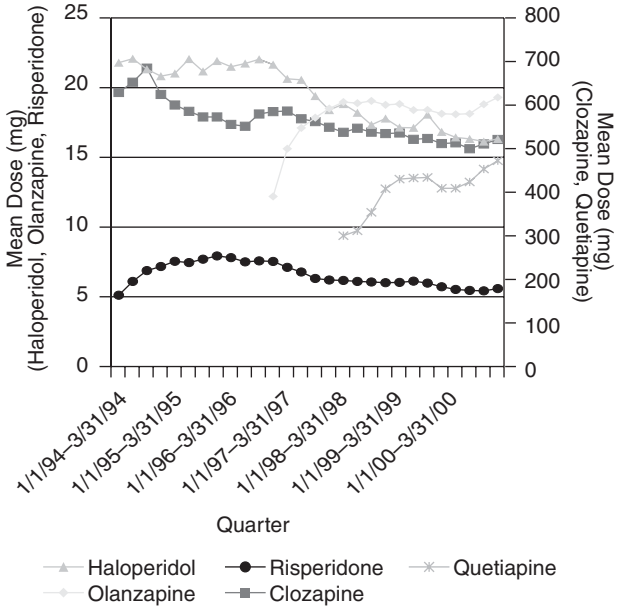


Figure 4. Dose Tends for Selected Antipsychotic Medications, 1994–2000.

## Coprescribing of Antipsychotic Medications

Over the study period, coprescribing (the simultaneous prescribing of more than one antipsychotic medication) increased more than threefold, from 11.4 percent of all prescribing episodes to 38.6 percent of all prescribing episodes (see figure 2). Figure 5 illustrates the *kinds* of antipsychotic coprescribing from 1994 to 2000. In 1994, coprescribing was overwhelmingly (89 percent) a combination of a typical agent with its conjugate depot preparation (e.g., haloperidol with haloperidol decanoate). By the end of 2000, the introduction of the atypical medications was reflected in a greater heterogeneity in the kinds of combinations encountered. Consistent with atypicals becoming the dominant antipsychotic class in use, combination therapy involving atypicals made up the majority of coprescribing episodes by the end of 2000. The most common pairing was an atypical with a typical agent.

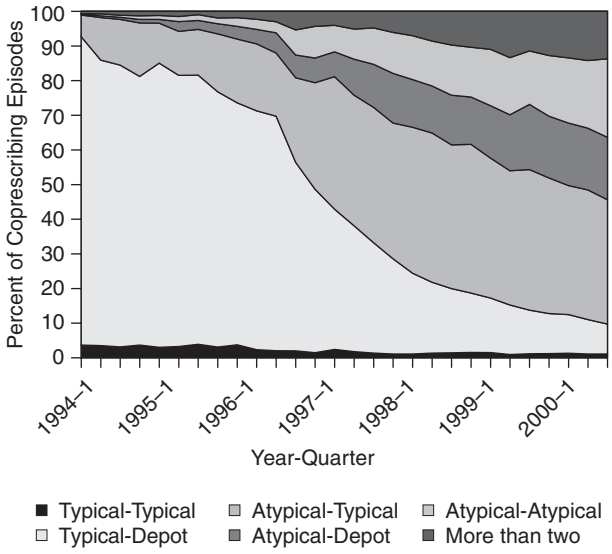


Figure 5. Kinds of Antipsychotic Coprescribing.

## Use of Augmentation Agents

Another important trend in prescribing for the hospitalized population with mental illness has been the increased use of augmentation agents, particularly anticonvulsant medications, in combination with antipsychotics. Valproate, the most commonly used of anticonvulsant augmentation agents, for example, has been shown to be an effective mood stabilizer, but its use extends beyond patients with a putative affective diagnosis (Citrome et al., 1998). This is illustrated in figure 6, which shows the percentage of antipsychotic medication episodes in the indicated year in which valproate augmentation was used, separated by patient diagnosis. For patients with schizophrenia, the prescribing of valproate in combination with an antipsychotic rose 25.5 percent over the period under study, although there is currently no approved Food and Drug Administration (FDA) indication for this use. In the

Table 2. Patients receiving antipsychotic medication in 1999

| | | Patients Receiving Antipsychotic Medication for at Least 7 Days (study sample) | | |
|---|---|---|---|---|
| | **Total Population Receiving Antipsychotic Medication, 1999** | **TOTAL** | **Admitted prior to 1999 ("Residents")** | **1999 Admissions ("Additions")** |
| Number of Unique Patients | 8,060 | 7,917 | 4,462* | 3,725** |
| Number of Patient Episodes (hospitalizations) | 8,899 | 8,589 | 4,466 (52.0%) | 4,123 (48.0%) |
| Gender | | | | |
| Male | 5,813 (65.3%) | 5,615 (65.4%) | 3,003 (67.2%) | 2,612 (63.4%) |
| Female | 3,086 (34.7%) | 2,974 (34.6%) | 1,463 (32.8%) | 1,511 (36.6%) |
| Mean Length of Stay | 1,162 days | 1,191 days | 2,205 days | 145.7 days |
| Age (years) | 44.4 | 44.4 | 46.6 | 42.1 |
| Number of Prior Admissions | 4.3 | 4.1 | 4.0 | 4.2 |
| Probability of Discharge from Hospital Within 1 Year | | | 39.5% | 82.5% |
| Diagnostic Distribution: (patients with indicated Dx as primary Dx of episode) | | | | |
| Schizophrenia (295.1, 295.2, 295.3, 295.6) | 4,047 (45.5%) | 3,942 (45.9%) | 2,293 (51.3%) | 1,649 (40.0%) |
| Schizoaffective (295.7) | 2,631 (29.6%) | 2,526 (29.4%) | 1,179 (26.4%) | 1,347 (32.7%) |
| Bipolar (296.4x, 296.5x, 296.6x, 296.7x, 296.8x, 296.0x) | 902 (10.1%) | 869 (10.1%) | 341 (7.6%) | 528 (12.8%) |
| Depression (296.2x, 296.3x) | 348 (3.9%) | 323 (3.8%) | 105 (2.4%) | 218 (5.3%) |
| Other or no Dx | 971 (10.9%) | 929 (10.8%) | 548 (12.3%) | 381 (9.3%) |
| ETHNICITY (terms are as coded in State patient database) | | | | |
| White | 47.9% | 47.7% | 49.0% | 46.3% |
| Black | 35.9% | 36.0% | 35.4% | 36.7% |
| Hispanic | 13.0% | 13.1% | 13.2% | 12.9% |
| Other | 3.2% | 3.2% | 2.4% | 4.1% |

* Four patients were erroneously listed in the database as having two simultaneous active admissions as of 1/1/99.
** Includes 270 unique patients who were in the hospital on 1/1/99 and had at least one subsequent discharge and readmission during 1999.

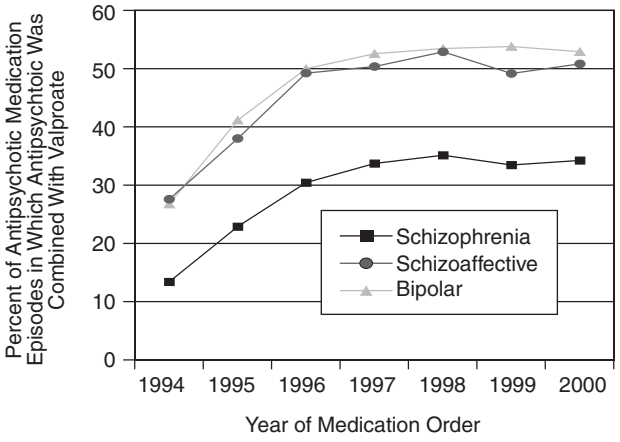


Figure 6. Augmentation With Valproate.

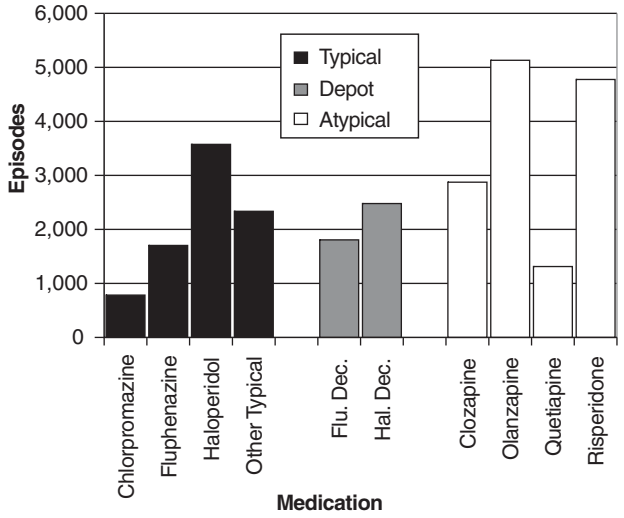


Figure 7. 1999 Antipsychotic Medication Utilization.

case of bipolar disorder (mania), there is an approved indication, so the high rates of prescribing illustrated for this patient population in figure 6 is best considered a "primary" rather than "augmentation" application of the medication.

## Relationship Between Prescribing Patterns and Patient Characteristics

To investigate the relationship between prescribing patterns and patient characteristics, we did a more detailed analysis of prescribing for 1999. By 1999, all three of the newer atypical medications considered here had been introduced and had been widely adopted. The year 1999 was also one of relative stability in the OMH system, with no hospital closures occurring during that year.

In 1999, of a total of 18,599 antipsychotic prescribing episodes, 7,718 (41.5 percent) were for patients admitted during 1999. Figure 7 illustrates the distribution of antipsychotic medications used during the year. Olanzapine, risperidone, clozapine, and oral haloperidol were the most frequently used medications.

Table 2 shows the demographic and diagnostic characteristics of OMH patients receiving antipsychotic medication during 1999. Most patients were male, White, and carried a diagnosis of schizophrenia or schizoaffective disorder. As noted (see Context/Study Population section), there were profound differences in length of stay and in the probability of discharge between patients admitted during 1999 and those already resident at the start of the year. We compared these two groups in terms of demographic and diagnostic variables. Newly admitted patients were slightly younger, slightly more likely to be female, slightly less likely to be White, and somewhat less likely to carry a diagnosis of schizophrenia than were resident patients. We compared medication utilization patterns for patients differing by diagnosis, gender, ethnicity, and admission status.

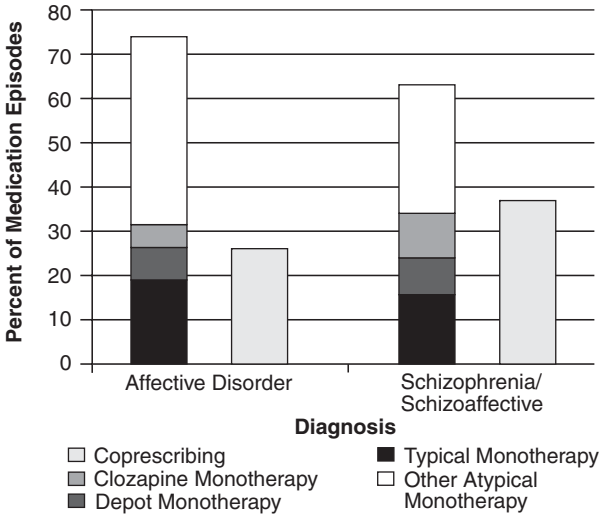


Figure 8. Antipsychotic Medication Utilization, 1999, Affective vs. Schizophrenic/Schizoaffective Diagnosis.

## Diagnosis

Figure 8 illustrates differences in antipsychotic use between patients with a primary diagnosis of schizophrenia or schizoaffective disorder and patients with an affective disorder diagnosis. The most prominent difference was the significantly[1] higher rate of combining antipsychotics (coprescribing) among patients with schizoaffective disorders and schizophrenia (36.9 percent vs. 26.1 percent among patients with affective disorder). When single-antipsychotic (monotherapy) episodes were examined separately, the most prominent finding was the significantly higher rate of clozapine use among schizophrenia and schizoaffective disorders.[2] By contrast, monotherapy with an atypical medication other than clozapine was somewhat less likely for schizophrenia and schizoaffective disorders than it was for patients with a diagnosis of affective disorder.[3]

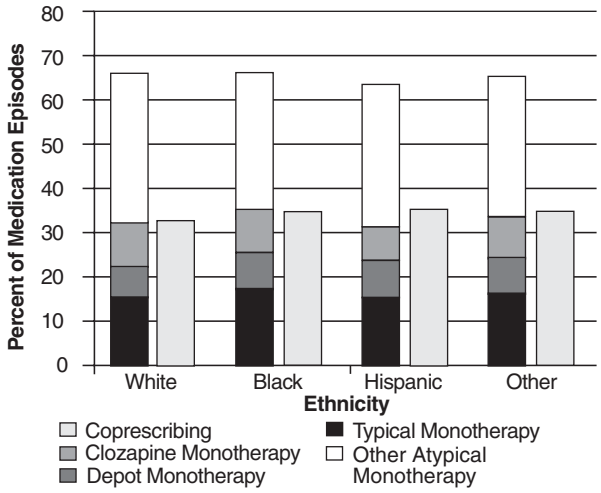


Figure 9. Antipsychotic Medication Utilization, 1999, Comparison by Ethnic Group.

## Gender and Ethnicity

There were no meaningful differences in use between men and women. Ethnic effects on use (figure 9) were statistically significant but were quantitatively modest. Black patients were more likely[4] than others to receive coprescribing (37.1 percent vs. 33.4 percent of prescribing episodes). When monotherapy episodes alone were considered, Black patients were more likely to receive oral typical and depot[5] agents and were correspondingly less likely to receive an atypical agent.[6] White patients, in contrast, were more likely than other ethnic groups to receive monotherapy with an atypical antipsychotic.[7] Hispanics did not differ significantly from non-Hispanics in regard to the likelihood of coprescribing or of receiving a particular monotherapy regimen. When ethnic group analyses were stratified by diagnosis to account for a slightly higher likelihood of the diagnosis of schizophrenia among Blacks, the reported ethnic differences still held, with the ethnic differences for the total population being accounted for by ethnic differences within the schizophrenia-schizoaffective diagnostic group alone.

## Admission Status

Because resident patients differ dramatically with regard to both their length of stay and likelihood of discharge from patients admitted in 1999, we were interested to see if there were any noticeable differences in antipsychotic medication use for this especially refractory group. Figure 10 illustrates the differences in use between patients resident in the hospital at the start of the year and those admitted during 1999. Although statistically significant differences between the two groups exist, the magnitude of the differences is small, with two exceptions: (1) markedly lower clozapine use among the newly admitted group[8] (clozapine monotherapy was 4.8 percent of all episodes vs. 12.3 percent for the resident group), and (2) somewhat higher antipsychotic coprescribing among the newly admitted group[9] (38.1 percent vs. 32.4 percent).

[1] $X^2 = 97.289$, df = 1, $p < .001$.

[2] $X^2 = 87.484$, df = 1, $p < .001$.

[3] $X^2 = 70.619$, df = 1, $p < .001$.

[4] $X^2 = 26.239$, df = 1, $p < .001$.

[5] $X^2 = 27.891$, df = 1, $p < .001$ for oral typical; $X^2 = 44.361$, df = 1, $p < .001$ for depot.

[6] $X^2 = 9.648$, df = 1, $p < .003$ for clozapine; $X^2 = 46.876$, df = 1, $p < .001$ for other atypical.

[7] $X^2 = 13.236$, df = 1, $p < .001$ for clozapine; $X^2 = 45.564$, df = 1, $p < .001$ for other atypical.

[8] $X^2 = 260.481$, df = 1, $p < .001$.

[9] $X^2 = 63.83$, df = 1, $p < .001$.

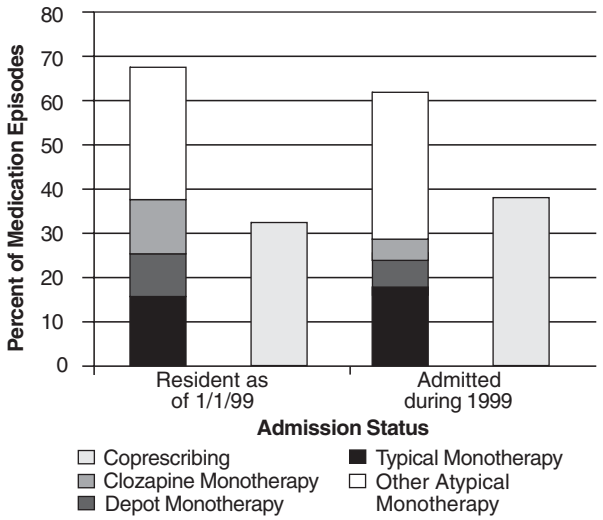


Figure 10. Antipsychotic Medication Utilization, 1999, Resident vs. Newly Admitted Patients.

### Valproate Augmentation

Because anticonvulsant augmentation was very common by 1999, we chose to examine whether it had an impact on antipsychotic coprescribing. Antipsychotic coprescribing occurred in 34 percent of episodes that used valproate, while it occurred in 32 percent of episodes that did not.

## Discussion

### Prescribing Trends

The period from 1994 to 2000 was characterized by two main prescribing trends with regard to antipsychotic medication utilization in this large State hospital system that has had no regulated formulary. First was a rapid introduction of the newer atypical medications, which have now effectively supplanted typical agents as the modal antipsychotic therapy. What is most notable about the introduction of the newer medications is that, with the introduction of each new atypical, the *total* use of atypicals increased. Thus, there was little apparent "cannibalization" of an older atypical by the introduction of a newer atypical. This was largely a consequence of the increased use of atypicals coming at the expense of oral typical monotherapy, as well as of increased coprescribing.

The changes in mean daily dose observed over the course of the introduction of the new medications are likely due to the net effect of many titrations as individual patients are started on a new medication, but may also represent the net effect of physicians developing clinical experience with the new drugs and finding "what works" for their patients. For risperidone, the decline observed in mean dose was likely a consequence of changed prescribing information recommending lower doses for that drug.

Second, from 1994 to 2000, the use of combination strategies—both of antipsychotic coprescribing and of augmentation with anticonvulsant agents, most commonly valproate—increased substantially. The increase in antipsychotic coprescribing, more than 300 percent from 1994 to 2000, is striking. Also notable is the marked change in the kind of coprescribing taking place. Before the wide-scale introduction of the atypical antipsychotics, coprescribing was usually due to the combination of an oral typical agent with its conjugate depot, a practice that has been shown to have some utility in improving the tolerability of depot regimens (Huttunen et al., 1996). By the end of 2000, however, the majority of coprescribing episodes combined an atypical medication with one or more other medications. As more atypical medications were introduced, a larger proportion of coprescribing has consisted of within-class (atypical-atypical) combinations and regimens using three or more antipsychotics simultaneously—two practices that add considerably to the expense of antipsychotic pharmacotherapy and have very limited published support. Although augmentation strategies, such as the use of valproate for patients with nonaffective illness, might be expected to obviate the need for antipsychotic coprescribing, the data do not support this presumption. Not only has coprescribing increased threefold over the same period in which valproate augmentation for schizophrenic patients has more than doubled, but in 1999, the inclusion of valproate in a medication regimen did not decrease the likelihood that multiple antipsychotics would also be used.

### Correlates of Antipsychotic Use

Although some patient characteristics were observed to correlate with antipsychotic prescribing patterns, there were very few marked differences. Potentially interesting findings were the observed differences in the use of clozapine and of antipsy-

chotic coprescribing. Both episodes using clozapine and coprescribing episodes were more likely among schizophrenic and schizoaffective patients than among patients with a diagnosis of affective disorder. This was not surprising given the generally more severe and refractory course of the former illnesses. What was surprising was the small magnitude of the differences between resident and newly admitted patients, who, by virtue of their very different lengths of stay and discharge probabilities, could be expected to differ in treatment responsiveness. Whereas clozapine use was more common among resident patients (consistent with the notion that the medication is used more often for the most refractory patients), coprescribing was *less* common among resident patients. This finding illustrates that antipsychotic coprescribing is not solely a strategy of last resort to which physicians are more likely to turn as patients remain in the hospital longer.

## Conclusion

Definitive data on antipsychotic prescribing practices for inpatients in a statewide system of psychiatric centers are scarce. Through the use of a unique research database containing orders filled and entered into a computer at every facility pharmacy combined with demographic and hospital data for every patient, we have been able to present a comprehensive description of prescribing practices over a seven-year period (1994–2000). Without aggregating and analyzing these prescription data, the dramatic changes in the antipsychotic medications being used could not be documented. The marked shift in use from typical to atypical medications and the rapid increase in coprescribing ("polypharmacy") of antipsychotic medications has caused pharmacy (medication) budgets to skyrocket. Various pharmacoeconomic analyses have attempted to show that overall costs of care have not increased because of the greater effectiveness of the new, but much more costly, medications. These studies should be augmented by combining the kind of medication utilization data presented in this chapter with associated clinical and outcomes data. This is a challenge for the future.

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